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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,254	TAREMI ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 14-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 14-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 1-5 and 14-33 are pending in the application.

[3] Applicant's amendment to the claims, filed on 12/21/2004, is acknowledged.

[4] The previous Office action mailed on 3/10/2005 is VACATED in favor of the instant Office action as agreed to in the interview on 6/30/2005. All rejections and/or objections set forth in the Office action mailed 3/10/2005 are withdrawn. New rejections and/or objections are presented below.

[5] Applicants are reminded of the revised amendment practice according to 37 CFR 1.121. The instant claim amendment uses an improper status identifier for claims 6-13 and 34-57. Also, the remarks section should begin on a separate sheet.

Election/Restriction

[6] Applicant's election of Group I, claims 1-5, 14-33, and 52-53, filed on 12/21/2004, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

[7] Claims drawn to non-elected inventions have been canceled by amendment.

Priority

[8] Applicants' claim to domestic priority under 35 U.S.C. 119(e) to US provisional applications 60/461,787, filed 4/10/2003 and 60/547,265, filed 2/24/2004, is acknowledged.

Oath/Declaration

[9] The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: There is no date of execution for inventor Jose Duca.

Examiner Comment/Clarification

[10] It is noted that the claims recite "the seven variable positions of SEQ ID NO:4. The seven variable positions of SEQ ID NO:4 are clearly defined in the specification at Table 1 (see pp. 23-24 of the specification).

[11] In view of the definitions of "Ac-^{6Cl}WAC$_{3c}$E" and "Ac-^{6Br}WAC$_{3c}$E" as being the compounds shown as a. or b., respectively, at p. 38, the examiner has interpreted the recitation of "Ac-^{6Cl}WAC$_{3c}$E" and "Ac-^{6Br}WAC$_{3c}$E" in claim 25 as being limited to a. or b., respectively. If applicants' intended meaning of these

terms is different from the examiner's interpretation, applicants are requested to so state and clarify the record.

[12] The examiner has interpreted the term "comprises 1, 2, 3...or 11 conservative amino acid substitutions" as being limited to no more than 11 conservative substitutions outside of the seven variable positions as shown in Table 1. Even though the phrase uses the open-ended transitional phrase "comprising," it is clear that the substitutions are limited to no more than 11. If applicants' intended meaning of this term is different from the examiner's interpretation, applicants are requested to so state and clarify the record.

[13] The examiner has interpreted the term "crystal effectively diffracts X-rays..." in claims 21-23 as meaning the crystal *does* diffract X-rays to a resolution greater than 5 Angstroms. If applicants' intended meaning of this term is different from the examiner's interpretation, applicants are requested to so state and clarify the record.

Claim Objection(s)

[14] Claims 5 and 20 are objected to in the recitation of "amino acid sequence of selected from the group consisting of.." It is suggested that applicants delete the first occurrence of "of" in line 3 of claims 5 and 20.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[15] Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 25 is indefinite in the recitation of "SCH549128" as it is unclear as to the compound that is referred to by "SCH549128." It is suggested that applicants clarify the meaning of the term.

[b] Claim 25 is indefinite in the recitation of "peptide derived from..." as it is unclear as to the amino acid sequences of the "derived" peptides. It is suggested that, for example, applicants identify the intended peptide sequences by structure and/or a sequence identifier.

[c] Claims 26 and 27 are confusing in the recitation of "crystal has the structural coordinates as set forth in Table..." as the structural coordinates of Tables 3 and 4 appear to be the structural coordinates of a polypeptide, and not a crystal. It is suggested that applicants clarify the meaning of the term.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[16] Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a polypeptide. The claims read on a product of nature and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[17] Claim(s) 1-3 and 15-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice,

reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The polypeptide of claims 1-3, 15-18, 21-25, and 28-32: Claims 1-3, 15-18, 21-25, and 32 recite a genus of polypeptides comprising SEQ ID NO:4, optionally having conservative substitutions. Claims 28-31 recite a genus of polypeptides that are characterized by structure coordinates comprising a RMSD of conserved backbone atoms of less than 2 Angstroms when superimposed on backbone atoms described by the structural coordinates of Table 3 or 4.

In this case, the specification discloses only four representative species of the genus of recited polypeptides, *i.e.,* SEQ ID NO:6, 8, 10, and 12. Other than these representative species, the specification fails to disclose any other additional representative species of the genus of claimed polypeptides, which encompasses species that are widely variant with respect to function, including species that are non-functional and species that have function other than the activity of SEQ ID NO:6, 8, 10, or 12. As such, the disclosure of the representative species of SEQ ID NO:6, 8, 10, and 12 is insufficient to be

representative of the attributes and features of all species encompassed by the claimed genus of polypeptides.

The crystal of claims 16-33: Claims 16-33 recite a genus of polypeptide crystals. The "Encyclopedia of Molecular Biology" (Creighton, T., John Wiley and Sons, Inc. New York, 1999, p. 586) states that "[i]n the regular packing inside the crystal, three repeating vectors can be recognized: a, b, and c, with angles α, β, and γ, between them. These three vectors define a unit cell in the crystal lattice." This same reference defines "unit cell" (p. 2725) as follows: "[a] crystal is characterized by the regular and periodic arrangement of its parts, which are ions, atoms, or molecules (see Crystallography). In this regular packing, three repeating vectors a, b, and c can be recognized with angles α, β, and γ between them." Also, the specification discloses "[t]he dimensions of the unit cell are defined by six numbers: dimensions a, b and c and angles α, β, and γ" (p. 10, bottom). See also p. 4, ¶ [0031] of US Patent Application Publication 2004/0005686 A1, which states, "[t]he dimensions of a unit cell of a crystal are defined by six numbers, the lengths of three unique edges, a, b, and c, and three unique angles α, β, and γ. The type of unit cell that comprises a crystal is dependent on the value of these variables and the various symmetry elements that are present within the unit cell." In view of the teachings of the specification and the prior art, the values of a, b, and c, with angles α, β, and γ are essential to describe the unit cell of a crystal. However, the claims fail to recite even a single structural feature of the claimed genus of crystals. In this case, the specification discloses only two representative species of the genus of claimed crystals, *i.e.,* a

crystal of SEQ ID NO:10 (Hdm2 F55Y/Y76H) co-crystallized with SCH549128 having the unit cell dimensions and space group symmetry as set forth at p. 46 of the specification and a crystal of SEQ ID NO:6 (Hdm2 Y76H) co-crystallized with Ac-^{6Cl}WAC$_{3C}$E having the unit cell dimensions and space group symmetry as set forth at p. 63 of the specification. Other than these two representative species, the specification fails to disclose the structures of any other members of the claimed genus, which encompasses crystals having any unit cell dimensions and space group symmetries. That the claims encompass species having widely variant structures is evidenced by Schubert et al. (US Patent Application Publication 2004/0197893) and Grasberger et al. (*J Med Chem* 48:909-912), which disclose crystals of HDM2 liganded with an inhibitor. The crystals of Schubert et al. and Grasberger et al. are distinct from the crystals as disclosed in the specification with respect to unit cell dimension, space group symmetry, and diffraction quality. Further, applicants' own specification shows that even crystals having only a single amino acid difference (SEQ ID NO:6 and 10) have distinct unit cell dimensions. As such, the two disclosed representative species fail to represent the variability within the genus and, consequently, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

The compound of claims 24-25: Claims 24-25 recite a genus of compounds that bind to a polypeptide, optionally wherein the compound is a peptide that is "derived from" the polypeptides recited in claim 25. As with the

genus of crystals, the claims fail to recite even a single structural feature of the recited genus of compounds. In this case, the specification discloses only two representative species of the genus of recited compounds, *i.e.,* the compounds as disclosed at p. 38 of the specification. Other than these two representative species, the specification fails to disclose the structures of any other members of the claimed genus, which encompasses compounds having any structure that have the ability to bind the recited polypeptide. As such, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Given the lack of description of a representative number of crystals, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[18] Claim(s) 1-3 and 15-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptides of SEQ ID NO:6, 8, 10, and 12, the compounds as disclosed at p. 38, a crystal of the purified polypeptide of SEQ ID NO:10 co-crystallized with SCH549128 having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=37.999 Å, b=45.333 Å, c=63.999 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays to a resolution of 1.70 Å and a crystal of the purified polypeptide of SEQ ID NO:6 co-crystallized with Ac-$^{6Cl}WAC_{3c}E$ having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=41.1 Å, b=42.7 Å, c=53.777 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays

to a resolution of 2.1 Å, does not reasonably provide enablement for the broad scope of polypeptides, compounds, complexes, and crystals as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: POLYPEPTIDES – the scope of polypeptides of claims 1-3, 15-18, and 21-32 are so broad as to encompass all polypeptides comprising a polypeptide having at least one mutation at position 11, 17, 39, 60, 65, 73, and/or 88 of SEQ ID NO:4 and up to 11 conservative amino acid substitutions that are not at one of the seven variable positions of SEQ ID NO:4, including polypeptides that do not have the desired activity/utility, *e.g.*,

polypeptides that are non-functional and are not biologically relevant for identifying inhibitors of p53 binding. The scope of claimed or recited polypeptides is not commensurate in scope with the enablement provided by the specification. In this case, the specification is enabling only for the polypeptides of SEQ ID NO:6, 8, 10, and 12. COMPOUNDS - the scope of compounds as recited in claims 24-25 is so broad as to encompass any compound that forms a complex with the polypeptide recited in claim 16, optionally limited to any peptide derived from the compounds as recited in claim 25. The scope of recited compounds is not commensurate in scope with the enablement provided by the specification. In this case, the specification is enabling only for the compounds as disclosed at p. 38. CRYSTALS – the scope of crystals of claims 16-33 encompasses crystals having any space group symmetry, any unit cell dimension, and having the ability to diffract crystals to a resolution as low as 1.5 Å. The scope of recited crystals is not commensurate in scope with the enablement provided by the specification. In this case, the specification is enabling only for a crystal of the purified polypeptide of SEQ ID NO:10 co-crystallized with SCH549128 having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=37.999 Å, b=45.333 Å, c=63.999 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays to a resolution of 1.7 Å and a crystal of the purified polypeptide of SEQ ID NO:6 co-crystallized with Ac-^{6Cl}WAC$_{3C}$E having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=41.1 Å, b=42.7 Å, c=53.777 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays to a resolution of 2.1 Å.

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: POLYPEPTIDES – the amino acid sequence of a polypeptide determines its structural and functional properties. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given nucleic acid were known in the art. However, neither the specification nor the state of the art at the time of the invention provide the necessary guidance for altering the nucleotide sequence of SEQ ID NO:6, 8, 10, or 12 with an expectation of obtaining a polypeptide having the desired activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York) teach "[p]rotein engineers

frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are exemplified by the reference of Witkowski et al. (*Biochemistry* 38:11643-11650), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647). COMPOUNDS – the structure of a compound determines its ability to bind and form a complex with a polypeptide. It is highly unpredictable as to which compounds, including any derivative of those recited in claim 25, would have the ability to bind and form a complex with the polypeptide as recited in, *e.g.*, claim 16. CRYSTALS – the state of the art at the time of the invention acknowledges a high level of unpredictability for making the full scope of claimed crystals. For example, the reference of Branden et al. ("Introduction to Protein Structure Second Edition", Garland Publishing Inc., New York, 1999) teaches that "[c]rystallization is usually quite difficult to achieve" (p. 375). In view of the use of the claimed crystal for generating a three-dimensional structure, it is noted that the claimed crystals should be of diffraction quality, having a well-ordered structure. Branden et al. teaches that "[w]ell-ordered crystals...are difficult to grow because globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and it is impossible to pack them into a crystal

without forming large holes or channels between the individual molecules" (p. 374).

The amount of direction provided by the inventor; The existence of working examples: POLYPEPTIDES – the specification discloses only four working examples of the claimed polypeptide, *i.e.,* SEQ ID NO:6, 8, 10, and 12. The specification fails to disclose any specific guidance for altering the SEQ ID NO:6, 8, 10, or 12 with an expectation that the resulting variants as encompassed by the claims will maintain the conformation of native HDM2 and have the ability to form co-crystals with the tripeptide inhibitor of p. 38 or any other compound as encompassed by the claims. COMPOUNDS – the specification discloses only two working examples of the recited compounds, *i.e.,* the compounds as disclosed at p. 38. The specification fails to disclose any specific guidance for making other compounds that have the ability to form a complex with SEQ ID NO:6, 8, 10, 12, or any other polypeptide as encompassed by the claims. CRYSTALS – the specification provides only two working examples of the claimed crystals, *i.e.,* a crystal of the purified polypeptide of SEQ ID NO:10 co-crystallized with SCH549128 having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=37.999 Å, b=45.333 Å, c=63.999 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays to a resolution of 1.7 Å and a crystal of the purified polypeptide of SEQ ID NO:6 co-crystallized with Ac-^{6Cl}WAC_{3c}E having the space group symmetry $P2_12_12_1$ and the unit cell dimensions of a=41.1 Å, b=42.7 Å, c=53.777 Å, $\alpha=\beta=\gamma=90°$ that diffracts x-rays to a resolution of 2.1 Å.

The specification fails to provide guidance regarding crystallization conditions of other polypeptides as encompassed by the claims optionally complexed with any compound.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of altering a protein's structure, methods of synthesizing compounds, and methods of protein crystallization were known in the art at the time of the invention, it is *not* routine in the art to: screen – by a trial and error process – for all polypeptides and compounds having a substantial number of modifications as encompassed by the claims for those polypeptides and compounds that have the desired activity/utility or crystallize a vast number proteins optionally complexed with any ligand under any crystallization conditions to make all crystals as broadly encompassed by the claims.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make all polypeptides, compounds, and crystals as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must

bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

[19] Claim(s) 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Kussie et al. (*Science* 274:948-953; cited in the IDS filed 8/30/2004).

The claims are drawn to crystals comprising a polypeptide "characterized by" structural coordinates comprising a RMSD of less than "about" 2.0, 1.5, 1.0, or 0.5 Angstroms of the backbone atoms of the structural coordinates of Table 3

or 4. It is noted that the instant rejection is made in view of the non-limiting terms "characterized by" and "about."

Kussie et al. teaches the preparation of crystals of MDM2 complexed with a p53 peptide (p. 953). This anticipates claims 28-31 as written.

Although it is acknowledged that the crystal of Kussie et al. has a different space group symmetry and unit cell dimensions relative to the crystal used to determine the structural coordinates of Table 3 or 4, the polypeptide of the claims is not limited to a polypeptide having structural coordinates comprising a RMSD of less than 2.0, 1.5, 1.0, or 0.5 Angstroms of the backbone atoms of the structural coordinates of Table 3 or 4 in view of the non-limiting terms "characterized by" and "about." Thus, absent evidence to the contrary, the reference of Kussie et al. teaches all limitations of the claimed crystal. Since the Office does not have the facilities for examining and comparing applicants' crystal with the crystal of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the crystal of the prior art does not possess the same material structural and functional characteristics of the claimed crystal). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[20] Claim(s) 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Schubert et al. (US Patent Application Publication 2004/0197893).

The claims are drawn to crystals comprising a polypeptide "characterized by" structural coordinates comprising a RMSD of less than "about" 2.0, 1.5, 1.0,

or 0.5 Angstroms of the backbone atoms of the structural coordinates of Table 3 or 4. It is noted that the instant rejection is made in view of the non-limiting terms "characterized by" and "about."

Schubert et al. teaches the preparation of crystals of HDM2 complexed with an inhibitor (p. 16, Example 2). This anticipates claims 28-31 as written.

Although it is acknowledged that the crystal of Schubert et al. has a different space group symmetry and unit cell dimensions relative to the crystal used to determine the structural coordinates of Table 3 or 4, the polypeptide of the claims is not limited to a polypeptide having structural coordinates comprising a RMSD of less than 2.0, 1.5, 1.0, or 0.5 Angstroms of the backbone atoms of the structural coordinates of Table 3 or 4 in view of the non-limiting terms "characterized by" and "about." Thus, absent evidence to the contrary, the reference of Schubert et al. teaches all limitations of the claimed crystal. Since the Office does not have the facilities for examining and comparing applicants' crystal with the crystal of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the crystal of the prior art does not possess the same material structural and functional characteristics of the claimed crystal). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Conclusion

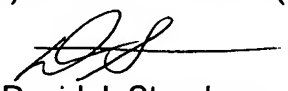
[21] Status of the claims:

- Claims 1-5 and 14-33 are pending.
- Claims 1-5 and 14-33 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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